LABELING

1 Device Labeling

1.1 Brief Device Description

The Kodak Mammography CAD Engine is a computer-aided detection (CAD) software package intended for use by radiologists to help identify regions of suspicion that may warrant a second review after the initial read of a mammogram. The Kodak Mammography CAD Engine is a proprietary software package to be used with the Kodak Case Input Station / for Mammography CAD System as well as a Kodak Report Station / for Mammography CAD System as accessories. All of these are designed to operate on standard computer hardware. The Kodak Case Input Station / for Mammography CAD System (CIS) also uses a high-resolution x-ray film digitizer. The Kodak Mammography CAD Engine, the CIS, the Report Station, and the high-resolution x-ray film digitizer constitute a complete CAD system.

The CIS allows x-ray mammograms to be digitized using the high-resolution film digitizer. The proprietary algorithm implemented in the Kodak Mammography CAD Engine then analyzes the resulting digitized image. The Kodak Report Station / for Mammography CAD System (RS) can be used to review the results of the algorithm in the form of specific CAD marks representing regions suspicious of signs of cancer, on low-resolution images. Alternatively, an equivalent report can be printed on paper.

The reading radiologist is instructed to first review each case in the usual manner without the use of the CAD marks. The radiologist is then instructed to review regions with CAD marks before concluding a final diagnosis for the case.

1.2 Indications for Use

The Kodak Mammography CAD Engine is a software package intended to identify and mark regions of interest on routine screening and diagnostic mammograms to bring them to the attention of the radiologist after the initial reading has been completed. Thus, the software assists the radiologist in minimizing observational oversights by identifying areas on the original mammogram that may warrant a second review.

1.3 Contraindications

There are no contraindications for this device.

1.4 Warnings

The likely users are technologists and radiologists. The technologist will typically be the primary user of the Kodak Case Input Station / for Mammography CAD System (CIS) with the film digitizer. The radiologist will typically be the only user of the Kodak Report Station / for Mammography CAD System (RS).

Warnings for the user of the Kodak Report Station / for Mammography CAD System

It is critical that the radiologist reviews the films in the conventional manner first, before reviewing the Kodak Mammography CAD System results. Reviewing the Kodak Mammography CAD System results before reviewing the films introduces the risk of the so-called satisfaction-of-search error, in which the radiologist fails to examine the unmarked areas of the films with adequate vigilance.

The Kodak Mammography CAD System responds to mammographic signs suggestive of masses and microcalcifications. It may not mark all regions that have other types of signs that are suggestive of cancer, such as small developing asymmetries. It also will not mark some masses and microcalcifications. *The lack of a mark should thus never lead the radiological interpreter to change a work-up decision arrived at during the unaided read.*

The software package may highlight areas that a radiologist will determine to not require work-up, at an average rate of approximately 1.0 mark per film (approximately 4.0 marks per 4-view mammogram). Thus, the work-up is determined by the radiologist, and the presence of a mark should not influence the decision that would have been made had the area been noted in the first place.

Kodak Mammography CAD System marks are not indicative of cancer. In fact, the majority of normal images will have marks. The device is intended only as an aid to detect suspicious regions that may warrant further review. The device is not intended to assess the likelihood of cancer of any region, marked or not.

Kodak Mammography CAD System may not mark the same lesion in both views.

The Kodak Report Station / for Mammography CAD System is not intended as a diagnostic reading device. The images presented on the RS are of very low resolution, unable to represent subtle signs of cancer, and only intended for anatomical reference of the regions marked as suspicious. Interpretations should therefore be performed on the films rather than on the monitor. Similarly, the printed Kodak Mammography CAD System report is not intended for diagnostic reading.

 No clinical studies have been conducted for patients with implants, and efficacy of the device for patients with implants has thus not been established.

Warnings for the operator of the Kodak Case Input Station / for Mammography CAD System

 Ensure and verify that films are digitized in the proper order and orientation (see user manual). Kodak Mammography CAD System may not detect all errors in order and orientation.

 Ensure that cases are properly identified to the system (using bar coding, see user manual).

 The high-resolution film digitizer is a critical component in the system in that it creates the input to the Kodak Mammography CAD Engine computer-assisted detection algorithm. Maintain the digitizer as specified, and operate in an environment as specified, in particular with reference to humidity.

 Follow regular quality control operations diligently. Only regular quality control of the digitizer will assure consistent quality and consistent computer-assisted detection algorithm operation.

 Use only film quality that meets standards defined by MQSA. Ensure that film is free of dirt, dust, marks, sticky labels, or any other material that may interfere with the digitization process.

 Do not place any objects (other than film) in or on the digitizer. Do not operate the digitizer wearing loose clothing (neckties, necklaces) that may become entangled in the feeding mechanism.

General warnings for operators of computing and digitizing equipment

 Kodak Mammography CAD Engine, CIS and RS are intended to be the only devices operating on the computing equipment on which they are installed. No other applications are to be installed.

 Access to CIS and RS is restricted by user name and password. Implement proper security procedures to control the management of user names and passwords to protect the device and the privacy of patient data.

 Operation of electronic equipment requires precautions to prevent electric shock. Never open any covers of any equipment. In the case of objects or liquids that may have fallen into the equipment, please unplug the equipment and contact authorized service personnel.

Only use grounded power sources for computing equipment. Use only grounded extension cables, and no adapters. Contact authorized service or installation personnel to solve any cabling problems. Keep cables out of the way to avoid tripping or damage to the cables.

Some computing equipment can radiate radio frequency energy. Do not operate such equipment where prohibited by the labeling of other medical devices that may be present.

Most computing equipment relies on proper ventilation. Do not cover any openings, and do not place any objects on computing equipment to avoid thermal problems.

1.5 Precautions

All users of CIS and RS should be trained by authorized Kodak personnel and should be familiar with the user manual prior to the first operation of the system. Radiological interpreters should be familiar with the principles of operations and the clinical studies as reported in the user manual.

Only two standard mammographic film sizes are supported: 18x24cm and 24x30cm.

Only four standard views per case (right and left cranio-caudal and medio-lateral oblique) are supported.

Barcodes are used for the identification of cases and patients. Proper use of existing barcodes (e.g. patient jacket identification number) should be confirmed with authorized Kodak personnel.

1.6 Adverse effects

There are no known direct risks to safety or health of the user or the patient that are related to the use of the device. Indirect inherent risks are: (a) that the device may not mark actionable areas; and (b) that the device may mark regions that are not actionable. These possibilities are clearly explained in the warnings included in the labeling of the device. Proper use of the marks generated by the device is explained in the directions for use of the device.

1.7 Summary of Pre-clinical Studies

This section describes pre-clinical, internal studies carried out by Kodak so that radiological interpreters may better understand how the device was developed in order to improve their understanding of the intended use and expected operation of the device.

1.7.1 CAD Algorithm Sensitivity and Specificity

During the development of the Kodak Mammography CAD Engine, over 2,000 cases with over 8,000 individual images were collected and digitized from five (5) mammography centers using a formal clinical protocol for algorithm development and validation purposes. The cases were randomly placed into one of three sets: training, testing, and clinical. The clinical cases were sequestered from software developers and were used in the clinical studies described in the next section. The software engineers to develop and test the Kodak Mammography CAD Engine in house used the training and testing sets. The sets consisted of biopsy-confirmed cancer cases and normal cases that had at least a two-year follow up confirmation of normality. Electronic truth was defined based on regions outlined by a site radiologist.

The algorithm was trained using data from the training set and then tested using the test set. Algorithm results were initially measured using different thresholds resulting in multiple sensitivity/false positive rate combinations. Bi-monthly test results were generated and analyzed to decide on the product-readiness of the device. The final benchmark showed a sensitivity of 93.8% with 0.88 false positive marks per normal image.

1.7.2 Comparison Study

It is widely accepted that performance measurements of a CAD algorithm is as much a function of the data as it is of the algorithm. To this end, a subset of the test and training databases at one site were analyzed using another commercially available CAD system. These results were compared to the marks generated by an early version of the Kodak Mammography CAD Engine on the same cases. The analysis was encouraging and provided useful reference data for further development.

1.7.3 Pilot Reader Study

In order to evaluate performance of the algorithm in the hands of a radiologist, a small reader study with two readers and about 80 cases was conducted. The study indicated that the marks made by the Kodak Mammography CAD Engine helped the radiologists to find more cancers than they identified in the unaided read.

1.7.4 Software Validation and Verification

Kodak has developed the Kodak Mammography CAD Engine in compliance with software standard AAMI/ANSI SW 68, Medical Device Software Lifecycle Processes. Validation of the Kodak Mammography CAD Engine is conducted as per the requirements of this standard.

1.8 Summary of Clinical Studies

This section describes clinical studies carried out by Kodak so that radiological interpreters may better understand how the device was developed in order to improve their understanding of the intended use and expected operation of the device.

A number of clinical pivotal studies and analyses were conducted to analyze precision and clinical performance of the Kodak Mammography CAD Engine:

The **Precision Study** had two objectives:

> **P1** Measure **sensitivity** of the CAD algorithm in isolation using biopsy-proven cancer cases; measure **false positive rate** on follow-up confirmed normal cases.
>
> **P2** Confirm **reproducibility** of the CAD algorithm in conjunction with the digitization process, using algorithm results based on repeated digitization of the same films on a group of different digitizers.

The **Reader Study** also had two objectives:

> **S1** Estimate the **increase in work-up rate**, resulting from the use of CAD, as compared to independent double reading by radiologists.
>
> **S2** Estimate the ability of the CAD algorithm, in the hands of a radiologist, to identify cancers earlier, based on their **performance on visible, actionable priors** (priors are mammograms temporally preceding the mammogram on which a cancer was found).

1.8.1 Precision Study-P1 (Sensitivity Study)

588 cases were collected and digitized from five (5) mammography centers using a formal clinical protocol. These cases are sequestered from the algorithm development group.

Biopsy-confirmed cancer cases were retrospectively collected using a randomized selection protocol. A number of exclusion criteria were applied to select only cases that had four views (two for uni-laterals), no implants, standard mammographic quality, sufficient patient information, etc. In addition, only densities in a size range of 5 to 50mm and only micro-calcification clusters of at least 3 micro-calcifications within a 6 mm circle were included.

The site radiologist identified the truth regions on film, and they were transferred into electronic form in XML format. This way, algorithm performance can be assessed automatically and objectively without human intervention. The site radiologist was also asked to identify each truth region as either a mass or a micro-calcification cluster. In addition, the site radiologist was asked to identify the primary sign of cancer for the case: "mass" or "MCC" (for "micro-calcification cluster"). Forty cases were labeled as both "mass" and "MCC." Of a total of 394 cancer cases, 262 were thus primary "mass" cases, and 172 were primary "micro-calcification cluster" cases, with an overlap of 40 cases.

Normal cases were also collected from the same five sites using a defined protocol. Similar exclusion criteria applied, but for normal cases, a confirming normal follow-up exam was required to exclude the possibility of the presence of undetected, developing cancer. 194 normal cases were thus added to the study, for a total of 588 cases in the study.

The Kodak Mammography CAD Engine was used to evaluate these 588 cases. A case was considered a true positive if a mark was placed on at least one cancerous lesion in at least one

view. Sensitivity was determined as the fraction of true positives over all cancer cases. False positives per image (FPi) were calculated as an average of false positive marks per image on all normal cases. The lower and upper bounds of the 95% confidence interval for sensitivity and FPi was determined using bootstrapping over cases (2.5% on each tail).

Table 1 - P1: Kodak Mammography CAD Engine Sensitivity

	Total	Detected by Kodak Mammography CAD Engine	Sensitivity	95% CI lower bound	95% CI upper bound
Primary "mass" cases	262	228	87.0%	83.1%	91.0%
Primary "MCC" cases	172	156	90.7%	86.0%	94.8%
All cases	394	344	87.3%	84.0%	90.6%

The average FPi was determined to be 1.0 false positive mark per normal image, with a 95% CI of +/- 0.1 FPi.

1.8.2 Precision Study-P2 (Reproducibility Study)

The algorithm implemented in the Kodak Mammography CAD Engine is digital, and since no physical source of variation or noise comes into play, it is expected to produce the same output every time it is presented with the same input. In contrast, the process of digitizing a film involves film positioning, and a delicate process of illumination and light quantum collection to reproduce a high range of optical densities at a high resolution with high fidelity. Invariably, subtle grey scale variations, as they are found in subtle lesions, will present with slight variation in digitized images. Reproducibility is thus expected to be higher for well-characterized lesions that are clearly visible in both views. The reproducibility study also analyzes reproducibility in relation to lesion characteristics.

Twenty-two cases, with one lesion visible in both views were selected from the clinical and testing data sets. These cases were digitized at least nine times each on three different digitizers. Eighteen of these cases were reported as true positives in the base-line run in study P1, the other four being false negatives for the algorithm. Six of these eighteen cases were detected by the algorithm in both views in study P1, the other twelve being detected only on one view.

Reproducibility was measured as the largest number of equal outcomes among the 30 runs (e.g. 27 true positives out of 30 have a reproducibility of 90%, as do 27 false positives out of 30). As Table 2 indicates, reproducibility increases as cases with poor baseline algorithm results are excluded.

Table 2 - P2: Kodak Mammography CAD Engine Reproducibility

	Number	Reproducibility	95% CI lower bound	95% CI upper bound
All cases	22	92%	87%	98%
Baseline TP	18	94%	88%	100%
Baseline both views	6	100%	100%	100%

Confidence intervals were determined using bootstrapping over cases, digitizers, and individual runs on the digitizers. As expected, the largest source of variance is the case set itself.

1.8.3 Reader Study

While the Precision Study was designed to measure the performance of the Kodak Mammography CAD Engine alone, the Reader Study was designed to measure performance of the Kodak Mammography CAD Engine in the hands of a radiologist. The study was conducted at two of the five sites, and only data from those two sites were used.

A set of 228 cases was composed of normal, current, and prior cases in the following fashion. A site radiologist reviewed all cancer cases with available prior exams from precision study P1 for the two sites. All information about the case (current, prior, patient jacket) was available at the review. The site radiologist then determined whether the biopsy-confirmed lesion on the current exam was retrospectively visible on the prior exam. In this manner, a total of 47 visible "prior" cases were included and available for the study. The prior exam was taken an average of 15 months (6-36 months) earlier than the current exam.

The remaining cancer cases for the two sites from precision study P1 were randomized, and an additional 29 "current" cases were included and available for the study for a total of 76 cancer cases. Additionally, 152 normal cases were collected at the two study sites.

Eight MQSA-qualified radiologists with between 4 and 14 years of experience participated in the study. These radiologists had read between 1,000 and 15,000 mammograms in the year preceding the study. The radiologists had not seen the cases before the study and were blinded to the proportion of cancer cases and the nature of the cases (however, they all evidently and reasonably expected a higher proportion of cancers than in a regular screening environment). The radiologists were given a training session on the mechanics of the study and then were given hands-on training with 14 cases. After assessing each case without and with CAD marks, the radiologist was shown the truth for each of these training cases.

During the study, the readers were first presented with the films without any additional information (except surgical scars), and were asked to provide a BIRADS rating for each breast. Next, the readers were presented with the CAD marks, and were again asked to provide an updated BIRADS rating. The readers were instructed that they could not reverse a diagnosis from positive to negative, as per the device instructions. Additional information was collected for specific analyses of the study and is detailed below as necessary.

1.8.4 Reader Study-S1 (Work-up Rate Study)

Double reading is a generally accepted method to increase the accuracy of mammography. In independent double reading, two radiologists independently read a case. If one or both of the radiologists recommend work-up, the case is recalled for further studies. An increased sensitivity is thus expected to be accompanied by an increased work-up rate. This study and analysis was designed to compare these increases for human double reading to computer-aided reading.

Unaided and aided sensitivity for individual radiologists was determined as that fraction of cancer breasts that received a BIRADS rating of 0, 4, or 5. False positive rate on normal cases (using one breast) was used to model work-up rate. The average sensitivity and false positive rates for individual readers including 95% CI intervals were determined using bootstrapping over cases and readers.

Eight radiologists had independently read all cases, resulting in 28 possible independent double reading combinations. The average sensitivity and false positive rates for double reads including confidence intervals were again determined using bootstrapping over cases and all 28 pairs of double readers.

Finally, the increase in sensitivity and false positive rate from unaided to aided double reading was determined by joint bootstrapping of all three methods over readers and/or pairs of readers. The increases for both aided and double reading are statistically significant.

Table 3 - S1: Kodak Mammography CAD System Work-up Rate Increases

	Sensitivity	95% CI Interval	False Positive Rate	95% CI Interval
Unaided Read	71%	59-83%	33%	19-47%
Double Read	85%	78-91%	50%	40-59%
CAD-aided Read	75%	64-86%	38%	25-52%

The false positive rate is higher than in a regular screening setting for a number of reasons, including increased diagnostic thresholds of the readers and lack of available patient information in the study. Also, the sensitivity is lower than in a regular screening environment because of the large proportion of prior cases.

The following tables show a sub-analysis of sensitivity for prior and current cancers

Table 4 - Sub-analysis of unaided and aided sensitivity

Sensitivity	Unaided	Aided	Change
All Data	71%	75%	4%
Priors	58%	63%	5%
Currents	91%	93%	2%

And for BIRADS 1 and 2 normal cases:

Table 5 - Sub-analysis of unaided and aided false positive rate

False Positive Rate	Unaided	Aided	Change
All Data	33%	38%	5%
BIRADS 1	23%	30%	7%
BIRADS 2	45%	49%	4%

Both double and aided read result in a statistically significant increase of sensitivity and false positive rate at a similar relative rate. As with double reading, a small increase in false positive rate (and thus work-up rate) resulting from CAD-aided reading is deemed acceptable given a commensurate increase in sensitivity and cancers found.

1.8.5 Reader Study-S2 (Inferential Study)

This part of the study and analysis was designed to infer what proportion of visible cancers that was missed could have been found earlier had the Kodak Mammography CAD Engine been used. Not all cancers that are visible retrospectively would be considered actionable by most radiologists. Those that were missed by the reading radiologist, and that would be considered actionable by most radiologists, and that were correctly identified by the Kodak Mammography CAD Engine constitute the subset where the Kodak Mammography CAD Engine could have helped the radiologist to identify a cancer earlier, to potentially save lives.

The study thus consisted of two parts: determination of actionability of prior cases; and estimation of Kodak Mammography CAD Engine performance on those cases.

The BIRADS ratings for the 47 prior cases were selected from the reader study. The subset of the eight radiologists that had assigned an unaided BIRADS rating of 0, 4, or 5 was determined for each case. A commonly used weighted averaging scheme was used to arrive at the weighted number of actionable cases: for example, a case deemed actionable by 3 out of 8 radiologists was weighted by a factor 3/8, etc.

Four radiologists were also asked to identify the lesion upon which they based their BIRADS 0, 4 or 5 rating. Basing actionability only on those suspicious regions that actually developed into cancer, and weighting these based on the assessments of four radiologists only, resulted in a 22.3 actionable cases.

BIRADS ratings for the same cases were also collected for the aided read, and a change in actionability was accepted if the change was based on a lesion that was correctly identified by the Kodak Mammography CAD Engine. In this manner, the number of actionable cases was increased to 23.8.

Kodak Mammography CAD Engine results for the actionable cases were then combined using the same weighted averaging scheme mentioned above. Similarly, the times between current and prior exams were averaged in a weighted manner. The conclusion is that a radiologist using the Kodak Mammography CAD Engine would have correctly identified 39.4% of visible prior cases. Therefore, at least 39.4% of missed cancers could have been diagnosed 14.8 months earlier with the help of the Kodak Mammography CAD Engine.

Table 6 - S2: Kodak Mammography CAD Engine Prior Analysis (4 readers, correct location)

	Cases Deemed Actionable	Weighted	Identified by Kodak Mammography CAD Engine	Weighted
0 out of 4	6	0.0	1	0.0
1 out of 4	11	2.8	5	1.3
2 out of 4	14	7.0	10	5.0
3 out of 4	8	6.0	7	5.3
4 out of 4	8	8.0	7	7.0
Total	**47**	**23.8**	**30**	**18.5**
				39.4%

A 95% confidence interval of +/- 14% was determined by bootstrapping over readers and cases.

1.9 Conclusions drawn from Clinical Studies

The clinical precision studies measured the sensitivity of the Kodak Mammography CAD Engine at 87% (CI 84.0-90.6%) on all cancers, with a false positive rate of approximately one mark per image.

The clinical reader studies further demonstrated that use of the Kodak Mammography CAD Engine would have helped the radiologist to identify 39.4% (CI +/- 14%) of missed cancers 14.8 months earlier.

The work-up rate is necessarily increased because the Kodak Mammography CAD Engine is intended to alert radiologists to additional regions of interest, and not to reverse any unaided findings. In relation to the sensitivity improvement, the work-up rate increase is comparable to independent human reading.

1.10 Principles of Operation

The computer-assisted detection algorithm implemented in the Kodak Mammography CAD Engine is designed to detect two primary signs of cancer in mammograms: micro-calcification clusters (MCCs) and distinct densities (masses).

First, the algorithm identifies the breast region in the mammogram images to restrict the detection area for potential regions of suspicion. The tissue signal strength, breast shape and location of the resulting area are used as quality control measures, and may lead to the rejection of poorly scanned or improperly oriented mammogram films.

Second, an exhaustive set of initial cancer candidates is identified based on some general criteria. Examples of such criteria are, for masses, the tissue density (intensity) contrast and size, and, for MCCs, the presence of a cluster of high intensity spots. Next, a set of features based on the form, size, density and radiating spiculation are extracted from these candidates. Then, the likelihood of malignancy of each candidate is established by a classifier, which includes a cascade of neural networks and a rule-based decision tree. Finally, additional rules governing the maximum number of candidates per case, per breast, per image, and per type of lesion are applied to limit the number of candidates that the Kodak Mammography CAD Engine presents as CAD marks. These rules are sophisticated, but generally limit the number of the combined mass and MCC CAD marks to 10 per case, 6 per breast and 4 per view.

1.10.1 Masses

For masses, isolated dense regions with an equivalent diameter between 5 mm and 50 mm are identified and selected as initial candidates.

Several dozen features of the region immediately surrounding each candidate and also global characteristics of the breast are extracted as features for the candidate. These features were developed by qualitatively correlating them with histology, as well as from radiologists' experience. Specifically these features include the tissue pattern around the candidate (i.e., super-pixel features), radiating structure (i.e., number of spiculations, spiculation length and distribution), central density signal strength, border, shape, size and anatomical location (such as inside breast tissue or pectoral muscle region, or relative to the skin-line and chest-wall).

The classifier determines a numerical value, or rank, for each candidate. The classifier includes two neural networks and a rule-based decision tree. The algorithm as the likelihood of malignancy interprets the rank value for that candidate. The candidates are then examined for their relative rank within a view, a breast, and a case (of two breasts), and only the most likely malignant candidates are kept according to the maximum number of candidates to use. These final candidates are presented as CAD marks with a hollow circle on the Kodak Report Station / for Mammography CAD System or a paper printout.

Mark location: The CAD mark is usually located at the densest point of a density area. Thus the mark may not appear at the center of a central mass, as shown in Figure 1.

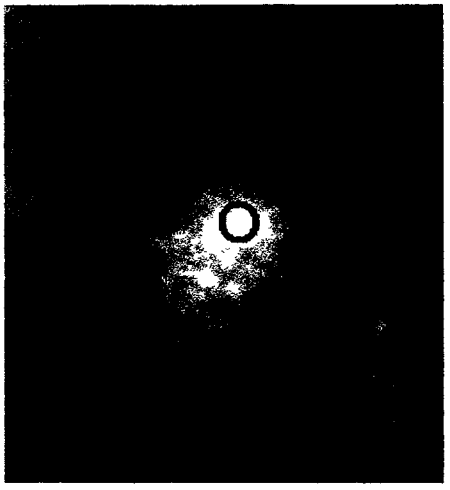

Figure 1 Mass Mark Location

Limitations: The algorithm uses a limited number of frequency bands to search for density regions, and may therefore not reliably detect very small or very big masses. The detection size range is designed for mass lesions between 5 mm and 50 mm. The algorithm also searches for distinct masses that present a central mass density. Therefore the algorithm has reduced sensitivity to masses with low contrast and weak signal.

False Alarms: The algorithm makes use of distinct density and associated radiating structures, so a mark may be on normal tissue with strong line signals or high intensity contrast, as shown in Figure 2.

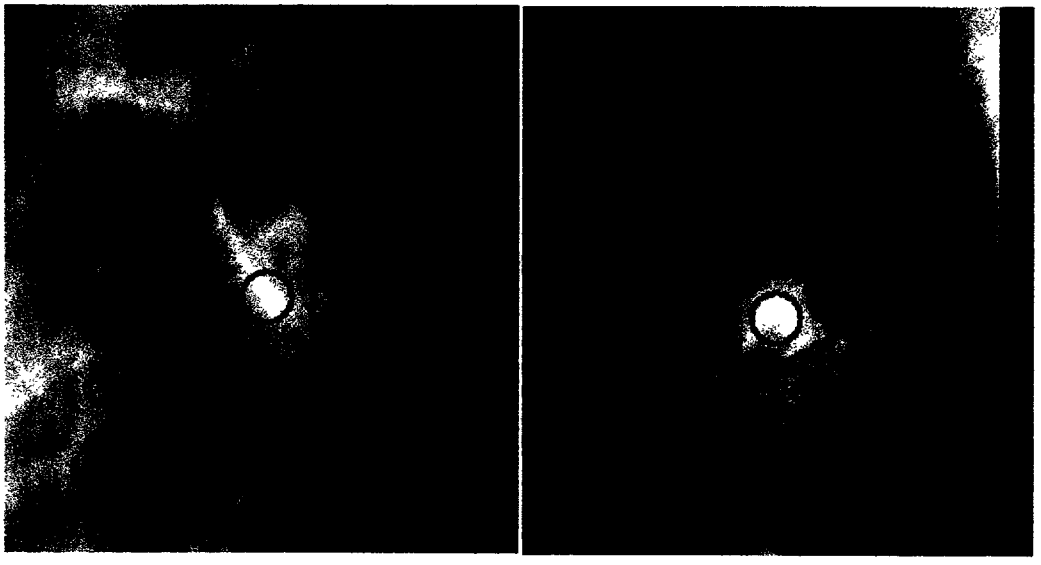

Figure 2 False Positive due to line signal and density contrast

1.10.2 Micro-calcification Clusters

Micro-calcifications usually appear in mammograms as small bright spots, whose intensity is higher than the surrounding tissue. Cancer is indicated by a group of several micro-calcifications, commonly referred to as a micro-calcification cluster (MCC). MCC detection starts by finding clusters of brighter spots as initial candidates. A cluster contains a

number of micro-calcification spots with spot-to-spot distance less than 6 mm, and with each micro-calcification spot bigger than 0.2 mm and smaller than 0.6 mm in diameter. A cluster contains at least 3 micro-calcifications. The size of each cluster is usually smaller than 120 mm^2.

As with mass processing, several dozen features are extracted for each candidate. These features include the distribution of the micro-calcification spots and describe the form, size and density of each micro-calcification. The features also include global characteristics of the breast.

Each candidate is ranked in a similar fashion to the mass processing, using a classifier. The classifier includes a calcification neural network, a cluster neural network, and a rule-based decision tree. The candidates are then examined for their relative rank within a view, a breast, and a case (of two breasts), and only the most likely malignant candidates are kept according to the maximum number of candidates to use. These final candidates are presented as CAD marks with a hollow triangle on the Kodak Report Station / for Mammography CAD System or a paper printout.

Mark location: The CAD mark is calculated to be located at the centroid of the micro-calcification spots within a cluster. Thus the CAD mark may not be located at any one of the spots in the cluster. Since a cluster is usually smaller than 120 mm^2, there might be more than 1 CAD mark on a large group of micro-calcifications as shown in Figure 3.

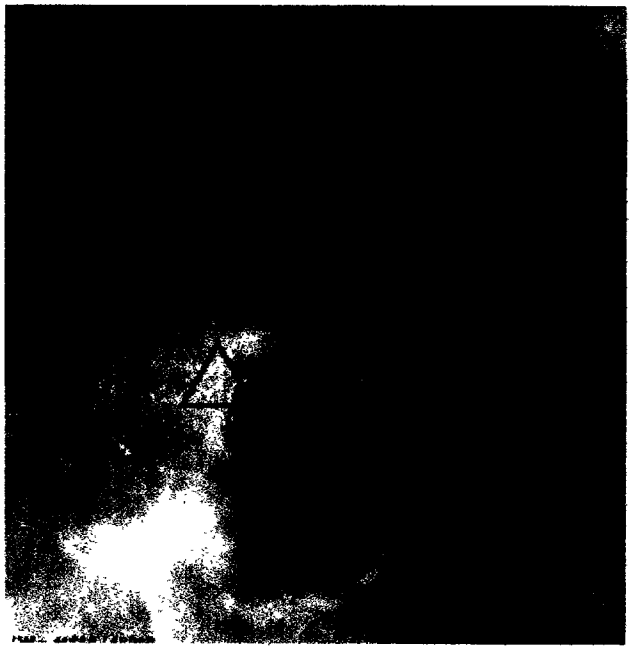

Figure 3 More than one mark on a large MCC

Limitations: The algorithm uses a set of typical criteria to detect micro-calcifications, specifically, assuming benign calcifications (not produced by a malignant process) are usually bigger than 0.6 mm in diameter, and film noise and skin calcifications are smaller than 0.2 mm in diameter. Therefore the algorithm has reduced sensitivity to very small or very big micro-calcifications. A cluster usually contains more than 3 bright spots, so the algorithm may not be sensitive to MCCs where some of the spots are very weak.

1.11 Conformance to Standards

The Kodak Mammography CAD Engine software package and its software accessories RS and CIS are installed on standard computing hardware which meets the requirements of the UL standard for Information Technology Equipment per UL1950 or UL60950 as well as the requirements of FCC Part 15 Class A.

The software package was developed in conformance to ANSI/AAMI SW68 Medical Device Software Lifecycle Processes.

1.12 How supplied

The Kodak Mammography CAD Engine software package and its accessories CIS and RS are installed by authorized Kodak personnel on off-the-shelf standard computing equipment (minimum configuration: Windows XP, 2GHz CPU, 500MB RAM, 20GB disk) together with an off-the-shelf medical high resolution x-ray film digitizer of at least 50 micron resolution and an optical density range of at least 3.6, also specified by Kodak.

1.13 Operator's Manual

The Kodak Mammography CAD System operator's manual is included here as an appendix.

1.14 References

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False Alarms: The main source of false positive marks is from arterial walls, hollow benign calcifications, and film artifacts appearing as bright spots. Some examples are shown in Figure 4.

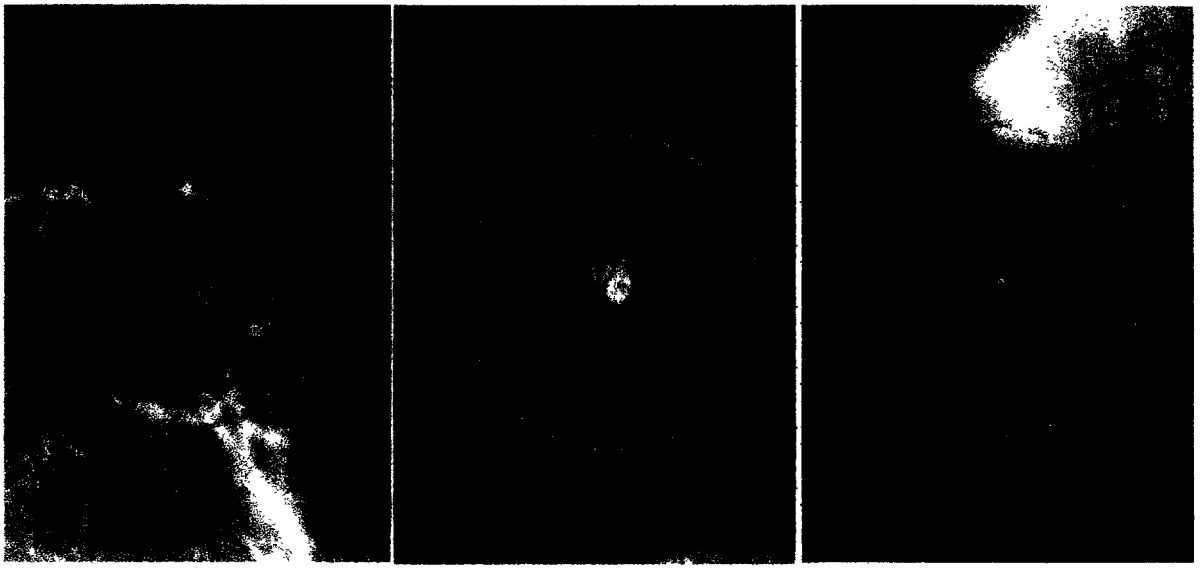

Figure 4 False Positive due to benign calcifications

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